REMARKS

I. Status of the Claims

Claims 11-14, 17-20, 34-36, and 40-45 are canceled

New claims 46 and 47 are added.

Claims 7-10, 15, 16, 28-30, 46, and 47 are pending. A complete copy of all pending claims is attached hereto.

II. Rationale and support for the Amendment

Claims 11-14, 17-20, 34-36, and 40-45 are canceled as being directed to a non-elected invention. Applicant expressly reserves the right to pursue the subject matter of these claims in one or more divisional and/or continuation applications.

Support for new claims 46 and 47 is found in the Specification at page 20, line 24 through page 21, line 12

III. Response to the Restriction Requirement

In the Restriction Requirement, the Examiner alleged that the present claims were directed to five groups of inventions, namely:

Group I: Claims 7-10, 15, 16, and 28-30, drawn to compositions and methods for treating cancer employing an enhanced combination of formulas IV and I or III.

Group II: Claims 11-14, drawn to compositions containing an enhanced combination of formulas IV and III.

Group III: Claims 17-20, drawn to a composition of formula I or III.

Group IV: Claims 40-45, drawn to a method for treating cancer employing formula IV alone.

Group V: Claims 34-36, drawn to a method for treating cancer employing an enhanced combination of formula I and III.

In response to the restriction requirement imposed by the Examiner, Applicant elects, without traverse, to prosecute claims 7-10, 15, 16, and 28-30, *i.e.*, the Group I claims.

As part of the Restriction Requirement the Examiner indicated that if Applicant elected Group I, he was further required to elect a "single enhanced combination of one compound of formulas I, III, and/or IV." In response to this requirement Applicant provisionally elects *sodium phenylacetate* as a specific compound of formula IV; *phenylacetylglutamine* as a specific compound of formula I; and *phenylacetylisoglutamine* as a specific compound of formula III.

The Examiner is invited to contact the undersigned patent agentat (713) 787-1589 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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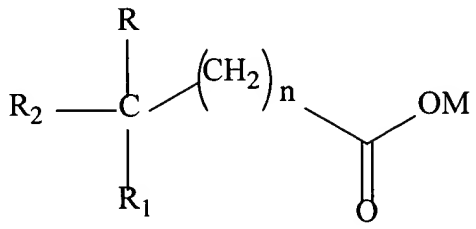
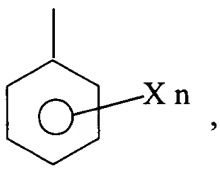
CLAIMS:

7. (Amended) A pharmaceutical composition, comprising in solution:

a compound of Formula IV:



wherein R and R_1 are independently selected from the group consisting of H, lower alkoxy (C_{1-6}), and lower alkyl (C_{1-6}); R_2 is selected from Formula II: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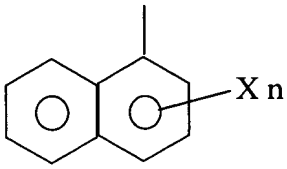
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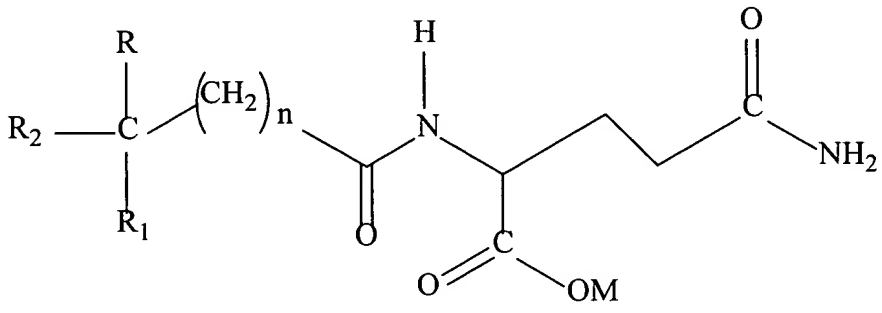
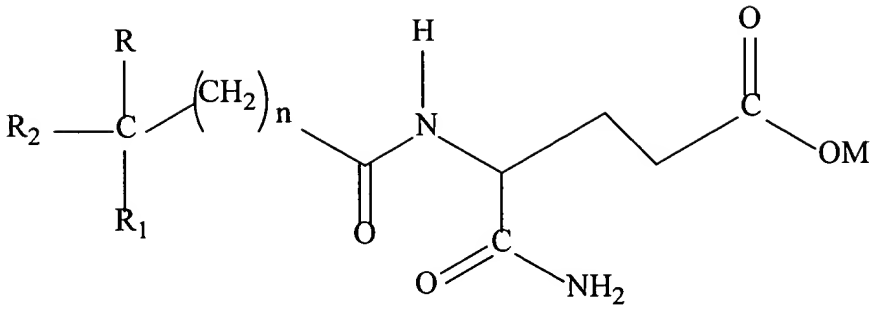
wherein X is a halogen, lower alkyl (C_{1-6}), lower alkoxy (C_{1-6}), cycloalkyl, cycloalkoxy, aryl (C_{6-12}), substituted aryl or hydroxy and n is 0, 1, 2, 3, or 4; M is hydrogen, a salt forming cation, alkyl (C_{1-6}), cycloalkyl, or aryl (C_{6-12}); and n is 0-5; and

a compound of Formula I:



or Formula III



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C_{1-6}), a cycloalkyl, or an aryl (C_{6-12});R and R_1 are independently selected from the group consisting of H, lower alkoxy (C_{1-6}), and lower alkyl (C_{1-6}); R_2 is selected from Formula II;

wherein the compound of Formula IV and the compound of Formula I are present in about a 4:1 ratio by weight; and

water sufficient to form an aqueous solution of the compound of Formula IV and the compound of Formula I wherein the combined concentration of the compound of Formula IV and the compound of Formula I is from about 70 mg/mL to about 150 mg/mL.

8. (Amended) The pharmaceutical composition of claim 7, wherein in the compound of Formula IV, M is hydrogen or sodium; n is 0; R is H or C_3H_7; R_1 is selected from the group consisting of H, CH_3, CH_3-O-, C_2H_5, and C_3H_7; R_2 is selected from Formula II, wherein X is Cl, F, or OH; and wherein in the compound of Formula I or III, M is hydrogen or sodium; n is 0; R is H or C_3H_7; R_1 is selected from the group consisting of H, CH_3, CH_3-O-, C_2H_5, and C_3H_7; R_2 is selected from Formula II, wherein X is Cl, F, or OH.

9. (Amended) The pharmaceutical composition of claim 7, wherein the compound of Formula IV is phenylacetic acid or pharmaceutically acceptable salts thereof, and the compound of Formula I is phenylacetylglutamine or pharmaceutically acceptable salts thereof, or the

compound of Formula III is phenylacetylisoglutamine or pharmaceutically acceptable salts thereof.

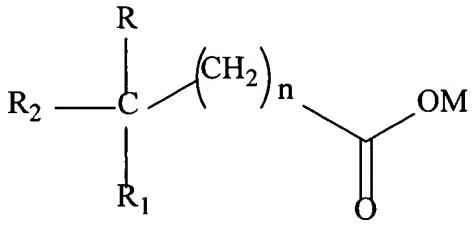
10. The pharmaceutical composition of claim 9, wherein the combined concentration is about 80 mg/mL.

15. (Amended) The pharmaceutical composition of claim 7, wherein the compound of Formula IV and the compound of Formula I or III are present in a 4:1 ratio by weight.

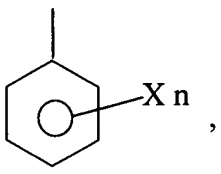
16. (Amended) the pharmaceutical composition of claim 7further comprising water sufficient to form an aqueous solution of the compound of Formula IV and the compound of Formula I or III wherein the combined concentration of the compound of Formula IV and the compound of Formula I or III is from about 70 mg/mL to about 150 mg/mL.

28. (Amended) A method of treating neoplastic disease, comprising:

administering to a patient at an infusion rate of from about 100 mL/hr to about 400 mL/hr of a pharmaceutical composition, the pharmaceutical composition comprising an aqueous solution of a compound of Formula IV:



wherein R and R_1 are independently selected from the group consisting of H, lower alkoxy (C_{1-6}), and lower alkyl (C_{1-6}); R_2 is selected from Formula II:



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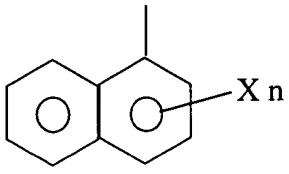

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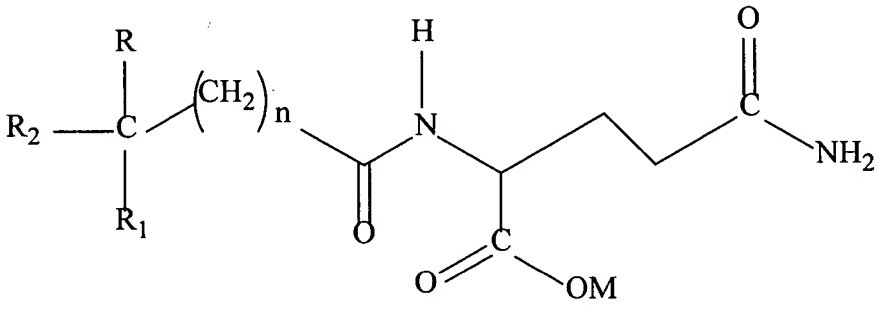
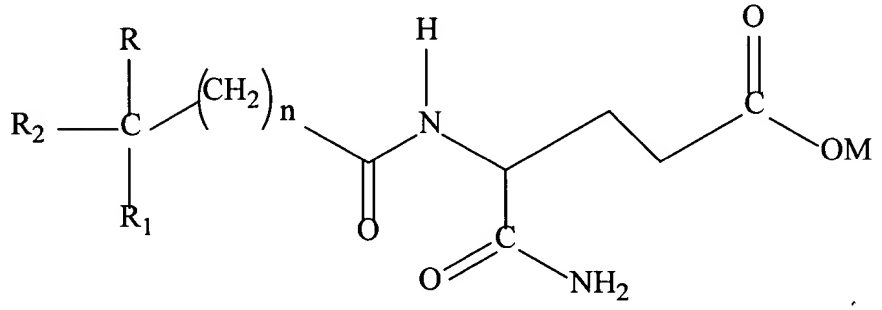
wherein X is a halogen, lower alkyl (C_{1-6}), lower alkoxy (C_{1-6}), cycloalkyl, cycloalkoxy, aryl, substituted aryl (C_{6-12}) or hydroxy and n is 0, 1, 2, 3, or 4; M is hydrogen, a salt forming cation, alkyl (C_{1-6}), cycloalkyl, or aryl (C_{6-12}); and n is 0-5; and,

a compound of Formula I:



or Formula III



wherein n is 0, 1, 2, 3, 4, or 5; M is hydrogen, a salt forming cation, an alkyl (C_{1-6}), a cycloalkyl, or an aryl (C_{6-12}); R and R_1 are independently selected from the group consisting of H, lower alkoxy (C_{1-6}), and lower alkyl (C_{1-6}); R_2 is selected from Formula II;

wherein the compound of Formula IV and the compound of Formula I or III are present in a 4:1 ratio by weight, and the combined concentration of the compound of

Formula IV and the compound of Formula I or III is from about 70 mg/mL to about 150 mg/mL.

29. The method of claim 28, wherein the infusion rate is about 250 mL/hr to about 300 mL/hr, and further comprising performing the administering step sufficiently often to reach a dosage level of from about 0.1 g/kg/day to about 2.6 g/kg/day.

30. The method of claim 29, wherein the dosage level is from about 0.2 g/kg/day to about 0.9 g/kg/day.

--46. **(New)** The method of claim 28 wherein the neoplastic disease to be treated is selected from the group consisting of cancer of a hard tissue, cancer of a soft tissue, a malignant tumor, and a benign tumor.

47. **(New)** The method of claim 28 wherein the neoplastic disease is selected from the group consisting of carcinoma of the adrenal gland, carcinoma of the bladder, carcinoma of the breast, high grade glioma, glioblastoma multiforme, anaplastic astrocytoma, low grade astrocytoma, brain stem glioma, primitive neuroectodermal tumors, medulloblastoma, pinealoblastoma, rhabdoid tumor of the central nervous stystem, oligodendroglioma, mixed glioma, neurofibroma, schwannoma, visual pathway glioma, ependymoma, germ cell tumors, meningioma, carcinoma of the colon, carcinoma of the rectum, carcinoma of the esophagus, primary liver cancer, metastatic liver cancer, carcinoma of the head, carcinoma of the neck, craniopharyngioma, choroid plexus neoplasm, adenocarcinoma of the lung, large cell undifferentiated carcinoma of the lung, bronchio-alveolar carcinoma of the lung, squamous cell carcinoma of the lung, nonsmall cell carcinoma of the lung, small cell carcinoma of the lung, Hodgkin's disease, non-Hodgkin's lymphoma, chronic leukemia, macroglobulinemia of Waldenstrom, mesothelioma, malignant melanoma, malignant fibrous histiocytoma, multiple myeloma, neuroblastoma, a neuroendocrine tumor, carcinoma of the ovary, carcinoma of the pancreas, a primitive neuroectodermal tumor outside the central nervous system, adenocarcinoma of the prostate, carcinoma of the kidney, Wilm's tumor, sarcoma, carcinoma of the small intestine, carcinoma of

the stomach, carcinoma of the uterus, carcinoma of the vulva, and carcinoma of an unknown primary.--